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INTERNATIONAL SEARCHING AUTHORITY

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1/9

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below
International application No. PCT/GB2005/000523	International filing date *(day/month/year)* 14.02.2005
Priority date *(day/month/year)* 13.02.2004	
International Patent Classification (IPC) or both national classification and IPC A61K35/36, A61K38/36, A61L27/60, A61P17/02	
Applicant INTERCYTEX LIMITED	

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Authorized Officer
European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Fuchs, U Telephone No. +49 30 25901-321

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2005/000523

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 36 (with respect to industrial applicability)

because:

☒ the said international application, or the said claims Nos. 36 (with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☒ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	4, 19-21, 24, 25
	No:	Claims	1-3, 5-18, 22, 23, 26-36
Inventive step (IS)	Yes:	Claims	21
	No:	Claims	1-20, 22-36
Industrial applicability (IA)	Yes:	Claims	1-35
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 36 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 02/072113 A (INTERCYTEX LIMITED), 19 September 2002

D2: EP-A-1 375 647 (CENTRO DE INVESTIGACIONES ENERGETICAS MEDIOAMBIENTALES Y TECNOLOGICAS), 2 January 2004

D3: TUAN, T.L. ET AL.: "In Vitro Fibroplasia: Matrix Contraction, Cell Growth, and Collagen Production of Fibroblasts Cultured in Fibrin Gels", EXPERIMENTAL CELL RESEARCH, vol. 223, 1996, pages 127-134, cited in the application

D4: MUHART, M. ET AL.: "Behavior of Tissue-Engineered Skin", ARCHIVES OF DERMATOLOGY, vol. 135, no. 8, August 1999, pages 913-918

1. Clarity, Support and Disclosure (Articles 5 and 6 PCT)

1.1 Claim 1 and dependent claims 2-36 relate to a wound healing composition comprising cells within a support matrix defined by reference to a desirable characteristic or property, namely "in which the cells have a wound healing phenotype".

The claims cover all cells having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such cells. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the cells by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to a wound healing composition comprising cells within a support matrix which has been incubated for up to about 8 days, as specified in claim 1.

1.2 In the working examples of present application (examples 1-3, pages 21-30), the manufacture of a wound healing composition is described, in which human dermal fibroblasts have been incorporated within a support matrix formed by thrombin-mediated polymerisation of fibrinogen, and in which the composition has been incubated for 16-24 h at 37°C.

However, no further kinds of cells, matrix components, or incubation conditions for the manufacture of the wound healing composition have been disclosed. Accordingly, the subject-matter of **claims 1-20, 22-36** might be regarded as not fully supported by the description in its entire scope, and, furthermore, not disclosed in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art. Analogous objections are to be expected in the regional phase.

2. Novelty and Inventive Step (Articles 33(2) and 33(3) PCT)

2.1 **D1** discloses a pharmaceutical composition, in which porcine dermal fibroblasts have been incorporated within a support matrix formed by thrombin-mediated polymerisation of fibrinogen, and in which the composition has been incubated for 24 h. The composition contains fibrin in a concentration of 6.75 mg per ml. It is used for the treatment of wounds.

In view of D1, the subject-matter of claims 1, 2, 5-16, 18, 22, 23, 26-36 is not novel.

2.2 **D2** discloses a pharmaceutical composition, in which human dermal fibroblasts have been incorporated in a human plasma based support matrix formed by thrombin-mediated polymerisation of fibrinogen, and in which the composition has been incubated for up to 14 days at 37°C. The composition contains protease inhibitors like aprotinin or tranexamic acid. It is used for the treatment of wounds. In view of D2, the subject-matter of claims 1, 3, 5, 7-12, 16-18, 22, 23, 26-36 is not novel.

2.3 In **D3** it is shown that dermal fibroblasts embedded and cultured for several days in a fibrin matrix show fibroplasia-like proliferation and collagen synthesis. Therefore, the subject-matter of claims 9, 10 is considered to be implicitly disclosed by the content of D1 and D2.

2.4 In the light of **D1-D3**, the subject-matter of **claims 1-3, 5-18, 22, 23, 26-36 lacks novelty**.

2.5 D1 is considered to represent the most relevant state of the art and discloses a pharmaceutical composition for the treatment of wounds, in which porcine dermal fibroblasts have been incorporated within a support matrix formed by thrombin-mediated polymerisation of fibrinogen, and in which the composition has been incubated for 24 h. The subject-matter of present application differs from D1 in that composition is stored after incubation for up to 40 days at a temperature of 2°C-8°C. However, this seems to be a standard procedure for a person skilled in the art. Accordingly, the subject-matter of **claim 4 appears to be obvious**.

2.6 Further, the subject-matter of present application differs from D1 in that the composition has a thickness of approximately 8 mm or less and comprises about 450-2,500 cells/mm^2. However, such a composition comprising human dermal fibroblasts embedded and cultured for several days in a fibrin matrix, having a thickness of approximately 2 mm and comprising about 2,000 cells/mm^2 has been disclosed in **D3**. As a consequence, the subject-matter of **claims 19, 20 does not involve an inventive step**.

2.7 Furthermore, the subject-matter of present application differs from D1 in that the composition is packaged in a container comprising a flexible pouch. However, the use of such flexible pouch containers for the packaging of wound healing compositions comprising fibroblasts has been disclosed in **D4**. Therefore, the subject-matter of **claims 24, 25 does not involve an inventive step**.

2.8 It is to be noted that the subject-matter of claim 21, representing what has actually been disclosed in the description, namely the manufacture of a wound healing composition, in which human dermal fibroblasts have been incorporated within a support matrix formed by thrombin-mediated polymerisation of fibrinogen, and in which the composition has been incubated for 16-24 h at 37°C, is considered to be novel and inventive.

3. Industrial Applicability (Article 33(4) PCT)

For the assessment of the present claim 36 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claim. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.